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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,761	01/21/2005	Tomi Jarvinen	HORMOS-019	2621

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EXAMINER	
GOON, SCARLETT Y	
ART UNIT	PAPER NUMBER
1623	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,761	JARVINEN ET AL.	
	Examiner	Art Unit	
	SCARLETT GOON	4131	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *21 January 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a National Stage entry of PCT/FI03/00511 filed on 24 June 2003 and claims priority to Finland foreign application 20021545 filed on 29 August 2002. A certified copy of the foreign priority document in Finnish has been received. No English translation has been received.

The preliminary amendment filed on 21 January 2005 in which claims 5-9 and 11-12 were currently amended, is acknowledged.

Claims 1-12 are pending in the instant application.

Information Disclosure Statement

The information disclosure statement (IDS) dated 21 January 2005 complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Accordingly, it has been placed in the application file and the information therein has been considered as to the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "lignan skeleton" in claims 1 and 5-6 renders the claims herein indefinite. The recitation of "lignan skeleton" for variable "L" suggests that the variable

represents the parent structure of a lignan compound. The Merriam-Webster online dictionary defines the term "skeleton" as "something reduced to its minimum form or essential parts". According to p. 8 of the specification, applicants indicate that "the lignan skeleton L ... stands for the part of the lignan molecule bearing such phenyl groups..." However, this is not considered a definition for the "lignan skeleton L" and also contradicts the generally accepted definition for "skeleton" since a skilled artisan looking at portion "L" of the structure would not immediately recognize it to have any features of a lignan. Upon evaluation of the lignan compounds in Scheme 1, p. 17, of the specification, Examiner concludes that L represents a substituted butyl linker that connects the two phenyl groups to form a lignan or lignan ester, while the lignan skeleton represents the two substituted phenyl groups connected by a substituted linker. Therefore, in order to advance prosecution, the claims will be interpreted herein as per Examiner's conclusions, and as apparently intended by applicant.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 5-8 and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by PG Pub No. 2005/0169947 by Korte *et al.*

Korte *et al.* discloses topical formulations comprising lignans or esters thereof as active ingredients, either for cosmetic or pharmaceutical use (p. 3, lines 9-11; p. 7, lines 24-25). The active agent, which is a lignan or a lignan ester, is selected from the group consisting of hydroxymatairesinol, lariciresinol, secoisolariciresinol, isolariciresinol, oxomatairesinol, α-conidendrin, liovil, picearesinol, syringaresinol or nortrachelogenin, or a lignan ester of formula (I) or (II) (page 3, lines 18-30). The topical formulation can be a liquid formulation, a semisolid formulation or a foam, shampoo, spray, patch, stick, batch additive or a sponge. The formulations can also be made as a liposomal formulation (p. 10, lines 26-27). The lignans or lignan esters can be entrapped in complexing agents, such as cyclodextrins, or polymeric vesicles with a shell consisting of a suitable polymeric material (p. 11, lines 9-13). Korte *et al.* further discloses that according to a preferred embodiment of their invention, the lignan or lignan ester is in the form of an inclusion complex with cyclodextrin (p. 11, lines 24-25).

The inclusion complex of a lignan or lignan ester with cyclodextrin, disclosed by Korte *et al.*, anticipates claims 1, 5-8 and 12.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in

the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Section [0001]

Claims 1-5, 7 and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,180,588 to Shinmen *et al.* (herein referred to as the '588 patent), US Patent No. 6,559,168 B2 to Marfat *et al.* (herein referred to as the '168 patent) and US Patent no. 6,395,279 B1 to Empie *et al.* (herein referred to as the '279 patent).

The '588 patent teaches a liver function improver comprising, as an effective ingredient, a dioxabicyclo[3.3.0]octane derivative. The dioxabicyclo[3.3.0]octane derivative has a structure of the general formula (I) (column 2, lines 9-30). The dioxabicyclo[3.3.0]octane compounds can be extracted from sesame oil, sesame lees, sesame seeds, *Acanthopanax sessiliflorus*, paulowina, Ginkgobiolobu, Piper lonum, and the like (column 3, lines 59-68), or it can be synthesized according to published protocols (column 4, 3-13). For example, a procedure for the synthesis of syringearesinol wherein R^1 and R^4 of general formula (I) represents H, R^2, R^3, R^5 and R^6 represents CH_3, n is zero, m is one, and l is one, is readily accessible (column 4, lines 9-13). The compounds can be used alone or in combination with other liver function improvers or as a functional factor of a food (column 4, lines 15-18 and lines 45-59). The compound can be administered orally or non-orally, such as by intramuscular injection, hypodermic injection or intravenous injection (column 4, lines 19-22). The composition can further contain an isotonic agent, a stabilizer, an antiseptic agent, and an analgesic agent (column 4, lines 36-38). If necessary, it can also be

formed into an emulsion, a capsule, dust, granule or tablet (column 4, lines 38-40) as a pharmaceutical composition that further comprises a pharmaceutically acceptable carrier (claim 1). Additionally, the compound can be converted to a cyclodextrin inclusion compound, and the formed powder can be used in a composition (column 5, lines 14-16). The '588 patent does not teach the different types of cyclodextrin available for use in the inclusion complex, nor does the reference teach a dietary supplement comprising the lignan complexed with cyclodextrin.

The '168 patent teaches thiazolyl-acid amide derivatives useful as inhibitors of PDE4 isoenzymes. There are many other types of PDE4 inhibitors, which also include lignans (column 17, lines 34-42). In order to improve the stability of the pharmaceutical compositions, sequestering agents such as cyclodextrins can be used. The cyclodextrins are a family of natural cyclic oligosaccharides capable of forming inclusion complexes with a variety of materials, and are of varying ring sizes, those having 6-, 7- and 8-glucose residues in a ring being commonly referred to as α-cyclodextrins, β-cyclodextrins, and γ-cyclodextrins, respectively (column 261, lines 16-23).

The '279 patent teaches a composition including saponogenins and saponins, lignans, phenolic acids, catechins and isoflavones and methods of using these compositions as nutritional supplements, dietary supplements or food additives (column 1, lines 13-19; abstract; claim 1). The composition can be delivered in an easy to consume dosage such as a pill, tablet, capsule, liquid or ingredient in a food including health bars (column 3, lines 45-48). The composition is intended to provide health and well-being benefits (column 4, lines 12-13) and is useful as a therapeutic treatment for

cancer (column 4, lines 64-67).It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the '588 patent, concerning a liver function improver comprising, as an effective ingredient, a dioxabicyclo[3.3.0]octane derivative, with the teachings of the '168 patent, regarding the use of cyclodextrins as sequestering agents, with the teachings of the '279 patent, regarding a composition including saponogenins and saponins, lignans, phenolic acids, catechins and isoflavones and methods of using these compositions as nutritional supplements, dietary supplements or food additives. One would have been motivated to combine the teachings in order to receive the expected benefit, as suggested in the '588 patent, and exemplified in the '168 patent, that cyclodextrins improve the solubility and stability of compositions. Additionally, as suggested in the '279 patent, lignans have health and well-being benefits, and are useful in treating cancer. Moreover, it would have been *prima facie* obvious for one of ordinary skill in the art to choose a cyclodextrin, from among the different types of available cyclodextrins, which is most suitable for the desired purposes, i.e. the specific lignan or lignan ester used may dictate the type of cyclodextrin used due to size constraints.

Absent of any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in preparing an inclusion complex of syringaresinol, or any other lignan, with the various types of available cyclodextrin compounds, for use as a nutritional or dietary supplement, as a functional food product, or as a pharmaceutical.

Section [0002]

Claims 1-4, 6-7 and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,413,533 B1 to Steiner *et al.* (herein referred to as the '533 patent), US Patent No. 6,559,168 B2 to Marfat *et al.* (herein referred to as the '168 patent) and US Patent no. 6,395,279 B1 to Empie *et al.* (herein referred to as the '279 patent).

The '533 patent teaches the chemoprevention of prostate cancer and a method of administering to a subject an effective dose of an antiestrogen agent to prevent prostate cancer and/or the recurrence of, suppression or inhibition of prostate carcinogenesis. Antiestrogens which act as prostate chemopreventive agents include, but are not limited to, toremifene and analogs, selective estrogen receptor modulators, triphenylethylenes, benzothiophenes, phytoestrogens, coumestrol, zearalenone, daidzein, apigenin, waempferol, phloretin, biochanin A, naringenin, formononetin, ipriflavone, quercetin, chrysin, flavonoids, coumestans, mycoestrogens, resorcyclic acid lactone, nafoxideneand equol, and lignans including enterodiol and enterolactone, etc. (column 4, lines 47-62). The parenteral formulation comprises a liposome comprising a complex of the antiestrogen and a cyclodextrin compound (claim 34). Alternatively, it may be a pharmaceutical preparation containing the active component, possibly delivered in a liposome (column 9, lines 57-58), along with excipients or other agents enhancing the effectiveness of the active ingredient (column 9, lines 21-22 and 33-26). The '533 patent does not teach the different types of cyclodextrin available for use in

making the liposome, nor does the reference teach a nutritional, dietary or food product comprising the composition.

The teachings of the '168 patent and the '279 patent were as discussed above in section [0001] of the claim rejections under 35 USC § 103.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the '533 patent, concerning a pharmaceutical preparation for the chemoprevention of prostate cancer that comprises a complex of an antiestrogen and cyclodextrin, with the teachings of the '168 patent, regarding the use of cyclodextrins as sequestering agents, with the teachings of the '279 patent, regarding a composition including saponogenins and saponins, lignans, phenolic acids, catechins and isoflavones and methods of using these compositions as nutritional supplements, dietary supplements or food additives. One would have been motivated to combine the teachings in order to receive the expected benefit, as suggested in the '168 patent, and exemplified in the '279 patent, that cyclodextrins improve the stability of compositions and that lignans have health and well-being benefits. Moreover, it would have been *prima facie* obvious for one of ordinary skill in the art to choose a cyclodextrin, from among the different types of available cyclodextrins, which is most suitable for the desired purposes, i.e. the specific lignan or lignan ester used may dictate the type of cyclodextrin used due to size constraints.

Absent of any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in preparing an inclusion complex of a lignan, in particular enterolactone or enterodiol, with the various

types of cyclodextrin compounds, for use as a nutritional or dietary supplement, as a functional food product, or as a pharmaceutical.

Section [0003]

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over PG Pub No. 2005/0169947 by Korte *et al.*, US Patent No. 6,559,168 B2 to Marfat *et al.* (herein referred to as the '168 patent) and US Patent No. 6,395,279 B1 to Empie *et al.* (herein referred to as the '279 patent).

The teachings of Korte *et al.* were as described above in the claim rejections under 35 USC § 102. Korte *et al.* does not teach the different types of cyclodextrin that may be used in forming the inclusion complex with lignans or lignan esters, nor does the reference teach a nutritional, dietary or food product comprising the composition.

The teachings of the '168 patent and the '279 patent were as discussed above in section [0001] of the claim rejections under 35 USC § 103.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Korte *et al.*, concerning a topical formulation comprising a lignan or lignan ester in a dermatologically acceptable vehicle for cosmetic or pharmaceutical use, with the teachings of the '168 patent, regarding the use of cyclodextrins as sequestering agents, with the teachings of the '279 patent, regarding a composition including saponogenins and saponins, lignans, phenolic acids, catechins and isoflavones and methods of using these compositions as nutritional supplements, dietary supplements or food additives. One would have been motivated to combine the

teachings in order to receive the expected benefit, as suggested in the '279 patent, and exemplified in the '168 patent, that lignans have health and well-being benefits and cyclodextrins improve the stability of compositions. Moreover, it would have been *prima facie* obvious for one of ordinary skill in the art to choose a cyclodextrin, from among the different types of available cyclodextrins, which is most suitable for the desired purposes, i.e. the specific lignan or lignan ester used may dictate the type of cyclodextrin used due to size constraints.

Absent of any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in preparing an inclusion complex of a lignan or lignan ester with the various types of cyclodextrin compounds, for use as a nutritional or dietary supplement, as a functional food product, or as a pharmaceutical.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Cecilia Tsang can be reached on 571-272-0562 and Janet Andres can be

reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cecilia Tsang/
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/SCARLETT GOON/
Examiner
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